ISSN No:-2456-2165

Phosphaturic Mesenchymal Tumor in Right Lower Limb: A Rare Case Report

Dr. Bhaskar V Musande, Dr. Narayan Sanap, Dr. Yashraj R Sapkal, Dr. B Naresh Kumar, Dr. Harsh Singh, Dr. Nikita Marathe, Dr. Shubham Tatu, Dr. Isha N Kedia

Abstract:- Phosphaturic mesenchymal tumor is a Tumor induced osteomalacia (TIO) which is a rare metabolic bone disorder due to renal phosphate wasting and abnormal production of FGF-23. Here we report a case of 26 year old male who presented with complaints of multiple joint pain and inability to walk with laboratory investigations suggestive of hypophosphataemia and a lesion in right lower limb causing TIO diagnosed by multidisciplinary approach. Patient underwent surgical excision with complete resolution of symptoms.

Keywords:- *Tumor induced Osteomalacia (TIO) , Fibroblast growth factor 23(FGF-23) , Hypophosphataemia.*

I. INTRODUCTION

26 Years Male patient presented to OPD complaining of multiple joint pain, and inability to walk since 3 years. The symptoms initially manifested as generalized weakness and multiple joint pain aggravated by walking. Over time, symptoms worsened to the extent that the patient had to use support for walking. The patient had a history of pathologic fracture neck of femur in 2020. The patient was admitted for the above complaints. The patient was initially screened for routine investigations which revealed hypophosphataemia (Sr. Phosphorous – 1.7 mg/dl), raised alkaline phosphatase (ALP-348 U/L) with normal calcium levels (Sr. Calcium - 9.5 mg/dl), and other parameters were within normal range. Based on the above report's patient was evaluated further for hypophosphatemia. Urinary calcium - 1.3 mg/dl, Serum PTH 69.1 pg/ml (Normal 12-88), Vit D3 – 35 ng/ml (Normal), Urinary phosphorous – 52.4 mg/dl, Urinary creatinine - 102.2 mg/dl, 24 hr urinary phosphorous – 464.1 mg/24 hrs (Normal - < 1100 mg/24hrs), with normal TFT. Ultrasonography of the abdomen is suggestive of the normal size of the kidney with corticomedullary differentiation. Both the RA factor test and HLA B 27 were negative. Based on the above laboratory investigations, TRP (Tubular reabsorption of Phosphorous) was found to be decreased. For Further evaluation of Hypophosphatemia and to rule out Tumor-induced osteomalacia, FGF 23(Fibroblast Growth Factor) and Gallium 68 DOTANOC PET-CT were done. It was suggestive of Increased FGF 23 - 772.1 RU/ml (normal 0-150) and PET CT revealed Increased Somatostatin receptor expression noted in the 13x10x16mm sized subcutaneous soft tissue density nodule in right lower leg seen anterior to the distal end of the shaft of right tibia (SUV max = 22.9), there was subtle erosion of cortex of tibia with osteoporotic changes in other bones suspecting this nodule to be the Culprit Tumor.

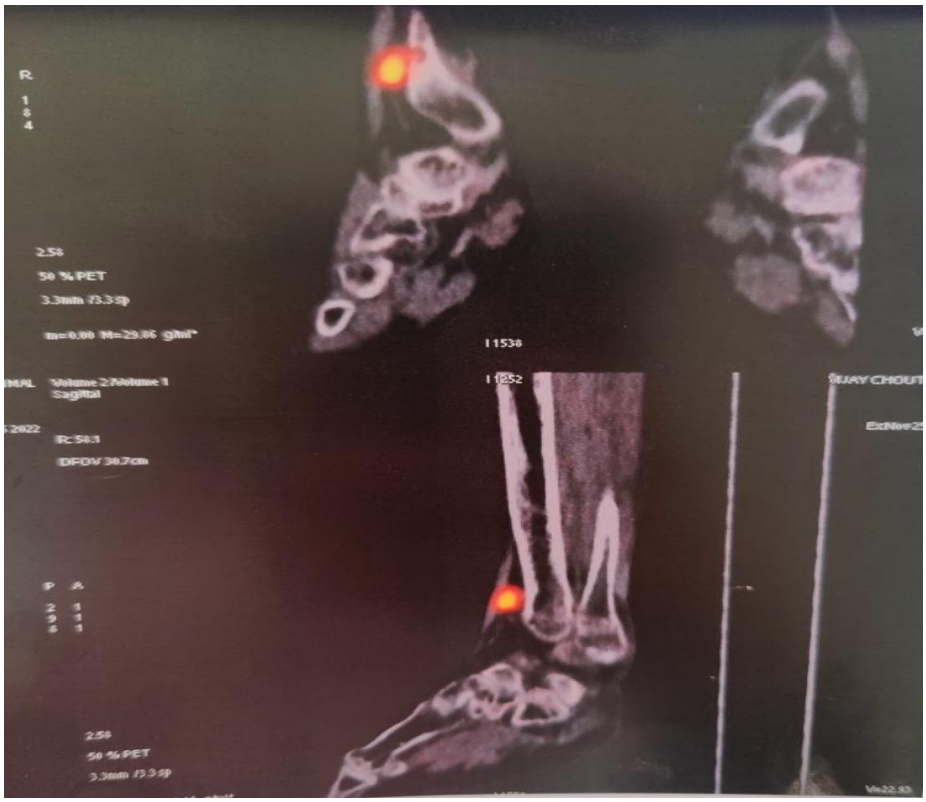

Fig. 1: PET CT showing Lesion in Right lower leg

Based on the PET CT report and on examination a solitary swelling of around 2x2 cm in right lower leg on the anterior aspect of the lower 1/3rd of tibia, with minimal tenderness and ill-defined margins. Contrast enhanced MRI (Right leg) s/o small relatively well-defined altered signal intensity lesion of 9x12mm in subcutaneous plane of anterior aspect of distal 1/3 of right leg showing homogenous post contrast enhancement with erosion of cortex of distal 1/3 of tibia with chronic stress fractures in talus, calcaneum, navicular, distal tibia and fibula.

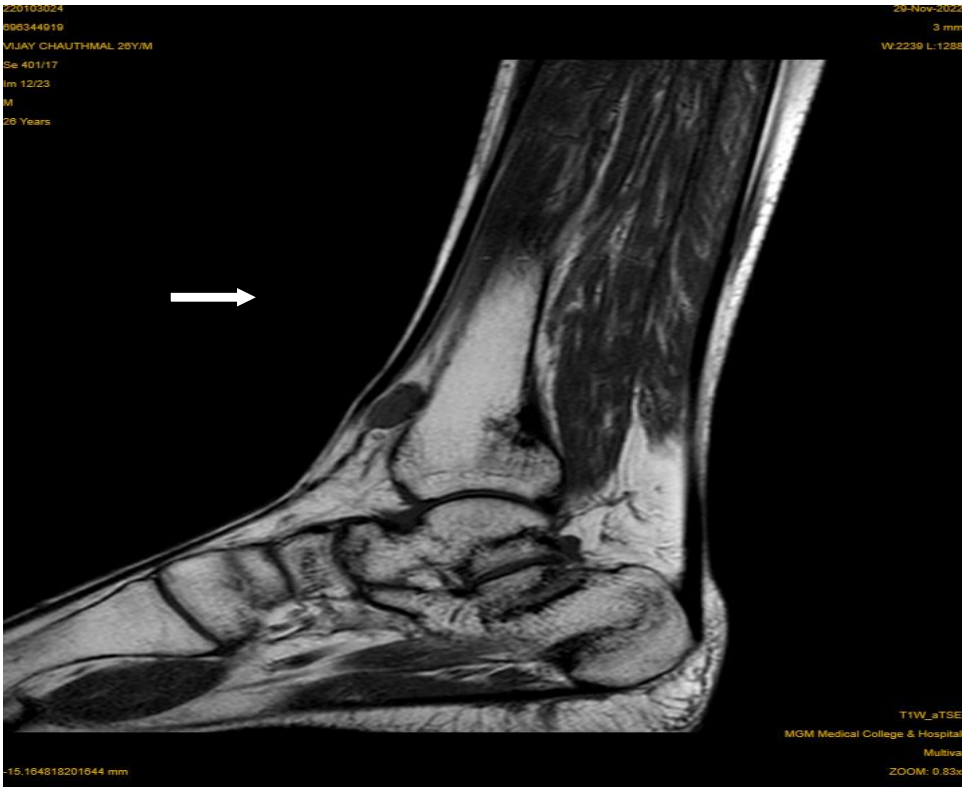

Fig. 2: T1W Image of Right lower limb showing Lesion on anterior aspect of tibia

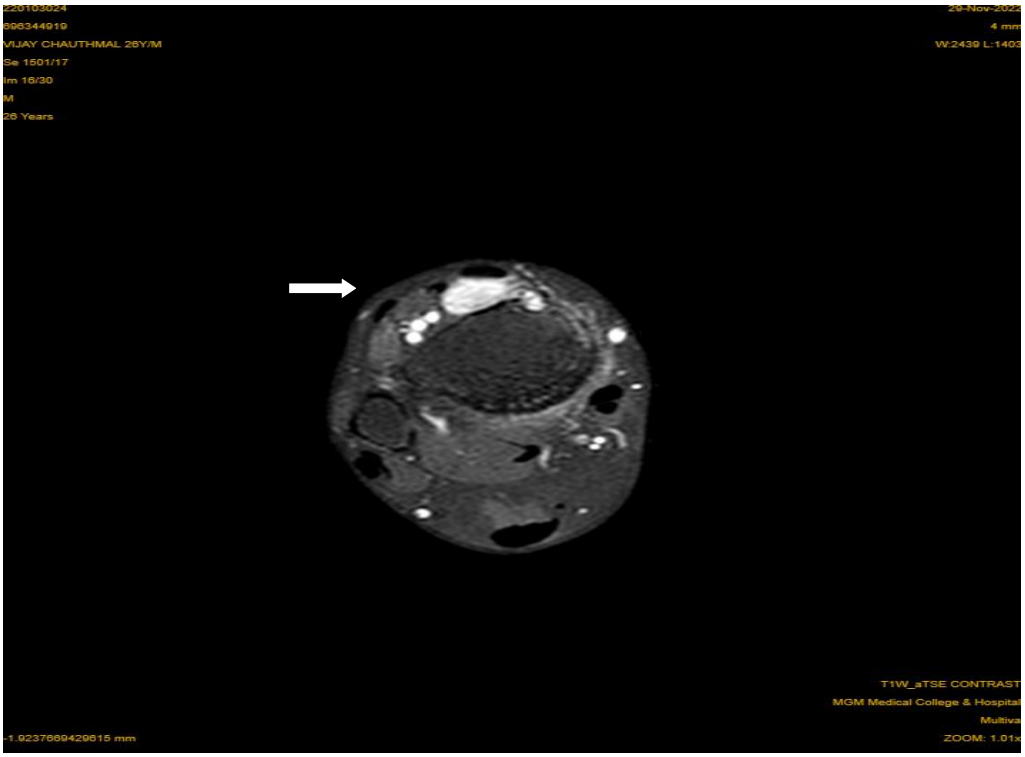

Fig. 3: T1W coronal image post contrast

ISSN No:-2456-2165

Patient was planned for elective surgery for exploration with wide local excision of lesion. Vertical incision was taken over the distal end of tibia on the anterior aspect. There was evidence of 2x1 cm well circumscribed, highly vascular lesion over the periosteum. Wide local excision with 1cm margin done. Specimen was sent for histopathological examination.

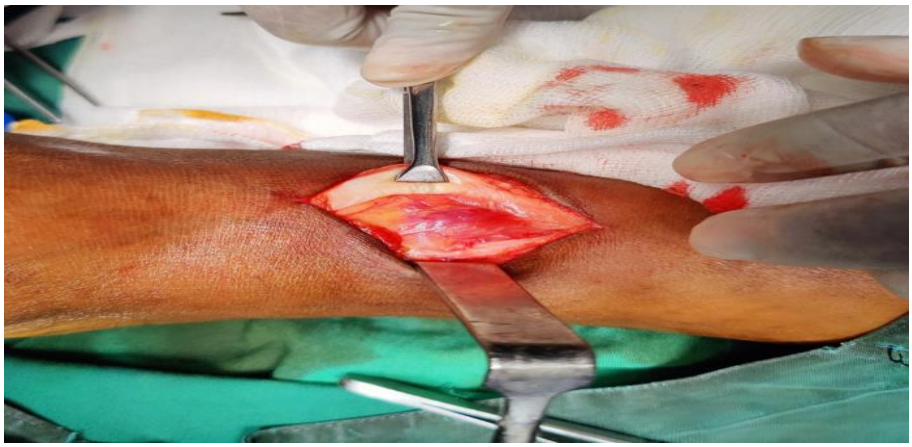

Fig. 4: Intra-operative image showing lesion over anterior aspect of tibia

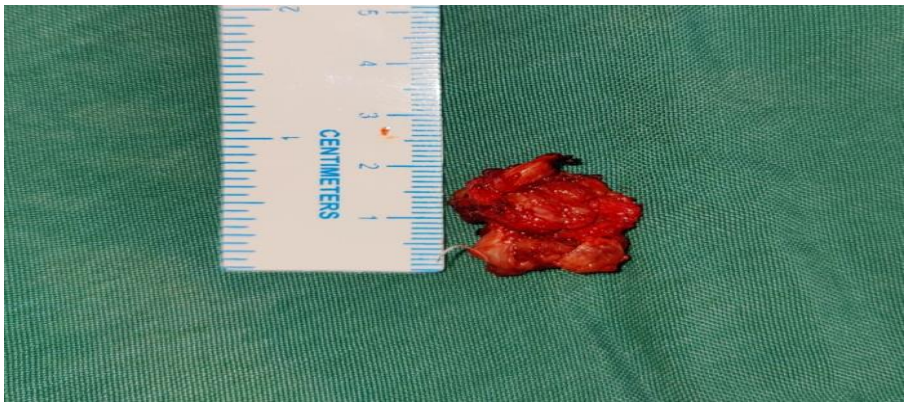

Fig. 5: Resected tumor

Gross specimen- A fibrous tissue measuring 2.3x1.5x1.5 cms which was extremely congested. On slicing there was an evidence of brownish fragile tumor measuring 1.6x1.5x1 cm.

Microscopy: section reveals benign neoplasm composed of spindle cells which are bland and arranged in sheets and fascicles and osteoclast type giant cells. Stroma is richly vascularised and consist of well devoloped capillary network and blood vessels arranged in staghorn / hemangiopericytoma like pattern, foci of cartilage and osteoid are also seen . All resection margins are free of tumor.

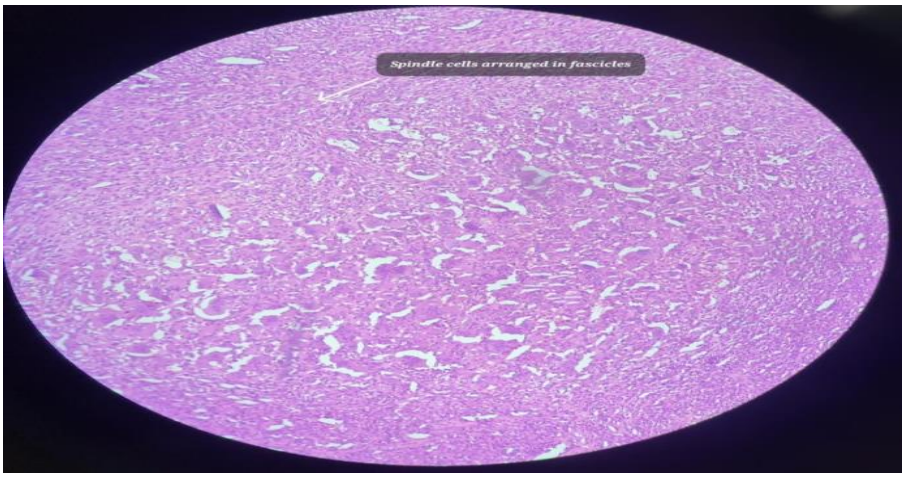

Fig. 6: showing spindle cells in fascicles

ISSN No:-2456-2165

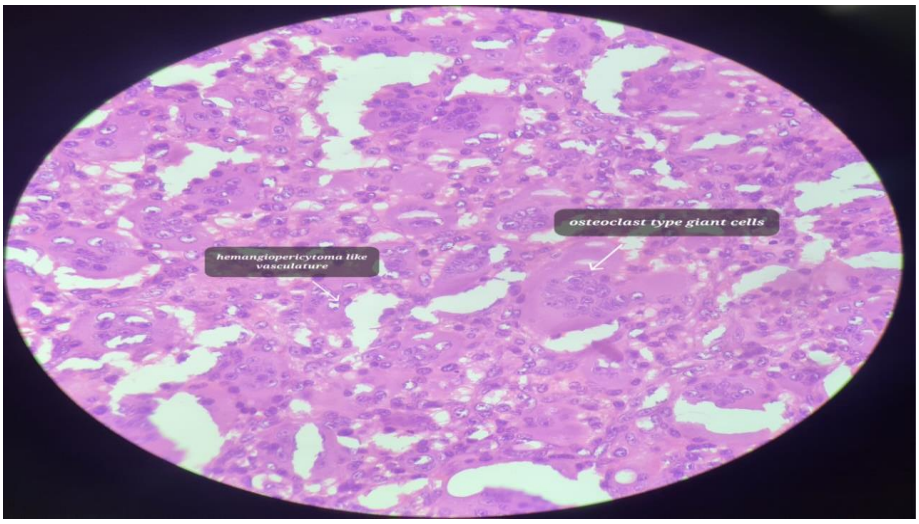

Fig. 7: showing osteoclast type giant cells and haemangiopericytoma like vasculature

Post operatively patient had resolution of symptoms and post operative laboratory investigations had returned to normal range (Sr. Phosphorous – 2.5 mg/dl and FGF 23 – 114 RU/ml)

II. DISCUSSION

Hypophosphaturic tumor is a tumor induced osteomalacia (TIO) which is largely under-diagnosed paraneoplastic condition. Being a rare metabolic bone disorder, TIO results from abnormal tumor production of FGF 23 resulting in isolated renal phosphate wasting.

Most commonly seen in males[1,2,3]. Predominantly seen at 45-55 years[1,4]. Tumor secretes phosphaturic factors (Phosphatonin) most common being FGF23. Tumor located commonly in extremities followed by head and neck and lastly in trunk and pelvis[1].

FGF 23 – produced by osteocytes and osteoblasts

⇩

Activates receptor complex of Fibroblast growth factor receptors 1C and co receptor klotho[5,14]

⇩

Reduces expression of Sodium phosphate co-transporters NaPi-IIa and NaPi-IIC

⇩

Inhibits tubular phosphate reabsorption at proximal renal tubule causing phosphaturia.

It also inhibits 1 alpha-hydroxylase enzyme and decreases 1,25-Dihydroxy Vitamin D production. Both these cause further impairment of intestinal absorption of phosphate[5].

Patient presents with bone pain (most common symptom)[4,6], muscle weakness, gait disturbance , height loss.

Stepwise approach is needed for identification and evaluation of hypophosphataemia as there is significant time gap from onset of symptoms to diagnosis. Median delay of 5.5 years for tumor > 5 cm and 3 years for < 5cm tumor was observed[1,7]. It begins with detailed history , family history for bone and mineral disorders and physical examination. The laboratory investigations includes serum phosphate , serum calcium , serum creatinine , urine phosphate , urine creatinine and PTH. TmP/GFR if less than 0.88 is indicative of TIO[5,8]. FGF-23 is the most specific and sensitive test in TIO (normal range is <120 RU/ml)[1,9,15]. Imaging is the next modality to precisely localize the tumor which includes MRI, CT scan and Ga-68 DOTATE , DOTANOC and DOTANOC PET-CT scan.[1,3,5,13]

Treatment includes supplementation of phosphate and calcitriol administration. Mainstay of treatment is surgical excision with wide margins[1,3,5,10]. Symptoms and laboratory parameters resolves rapidly post excision. Incompletely resected tumors are prone for recurrence and in such cases supplementation should be continued along with chemotherapy or radiotherapy.[11] Recurrence rate is 14.2% in surgically resected patients.[1,3,12]

III. CONCLUSION

TIO although rare paraneoplastic condition , is potentially treatable with multidisciplinary diagnostic approach[11] and surgical resection being the mainstay of treatment. In our case , patient with history of 3 years was evaluated and diagnosed to have a culprit tumor in Right lower leg which was successfully resected leading to improvement of symptoms clinically and also laboratory parameters.

ISSN No:-2456-2165

REFERENCES

[1.] Bosman, A. *et al.* (2022) "Tumor-induced osteomalacia: A systematic clinical review of 895 cases," *Calcified Tissue International*, 111(4), pp. 367–379. Available at: https://doi.org/10.1007/s00223-022-01005-8.

[2.] Ryan, E.A. and Reiss, E. (1984) "Oncogenous osteomalacia," *The American Journal of Medicine*, 77(3), pp. 501–512. Available at: https://doi.org/10.1016/0002-9343(84)90112-8.

[3.] Jiang, Y. *et al.* (2012) "Tumor-induced osteomalacia: An important cause of adult-onset hypophosphatemic osteomalacia in China: Report of 39 cases and review of the literature," *Journal of Bone and Mineral Research*, 27(9), pp. 1967–1975. Available at: https://doi.org/10.1002/jbmr.1642.

[4.] Aligail, K., Dave, J.A. and Ross, I.L. (2022) "Tumor-induced osteomalacia: A case report," *Journal of Medical Case Reports*, 16(1). Available at: https://doi.org/10.1186/s13256-021-03220-7.

[5.] Slot-Steenks, M.M. *et al.* (2016) "Identifying the culprit lesion in tumor induced hypophosphatemia, the solution of a clinical enigma," *Endocrine*, 54(3), pp. 642–647. Available at: https://doi.org/10.1007/s12020-016-1092-5.

[6.] White, K.E. *et al.* (2001) "Autosomal-dominant hypophosphatemic rickets (ADHR) mutations stabilize FGF-23," *Kidney International*, 60(6), pp. 2079–2086. Available at: https://doi.org/10.1046/j.1523-1755.2001.00064.x.

[7.] Minisola, S. (2020) "Review for 'burden of disease in patients with tumor-induced osteomalacia.'" Available at: https://doi.org/10.1002/jbm4.10436/v2/review2.

[8.] Bijvoet, O.L.M. and Morgan, D.B. (1970) "Plasma-phosphate and tubular reabsorption of phosphate," *The Lancet*, 295(7660), pp. 1345–1346. Available at: https://doi.org/10.1016/s0140-6736(70)91945-8.

[9.] Berndt, T.J. *et al.* (2005) "Secreted frizzled-related protein-4 reduces sodium–phosphate co-transporter abundance and activity in proximal tubule cells," *Pflügers Archiv - European Journal of Physiology*, 451(4), pp. 579–587. Available at: https://doi.org/10.1007/s00424-005-1495-2.

[10.] Li, Y. *et al.* (2019) "Comparison of surgical treatments of tumor-induced osteomalacia in different locations in the lower limbs," *Medicine*, 98(11). Available at: https://doi.org/10.1097/md.0000000000014846.

[11.] Chong, W.H. *et al.* (2013) "Tumor localization and biochemical response to cure in tumor-induced osteomalacia," *Journal of Bone and Mineral Research*, 28(6), pp. 1386–1398. Available at: https://doi.org/10.1002/jbmr.1881.

[12.] Folpe, A.L. *et al.* (2004) "Most osteomalacia-associated mesenchymal tumors are a single histopathologic entity," *The American Journal of Surgical Pathology*, 28(1), pp. 1–30. Available at: https://doi.org/10.1097/00000478-200401000-00001.

[13.] Thangavelu, T., Graeff-Armas, L. and Brau, K. (2019) "Mon-499 tumor induced osteomalacia: 68ga-dotatate PET/CT scan for localization," *Journal of the Endocrine Society*, 3(Supplement_1). Available at: https://doi.org/10.1210/js.2019-mon-499.

[14.] Urakawa, I. *et al.* (2006) "Klotho converts canonical FGF receptor into a specific receptor for FGF23," *Nature*, 444(7120), pp. 770–774. Available at: https://doi.org/10.1038/nature05315.

[15.] Feng, J. *et al.* (2017) "The diagnostic dilemma of tumor induced osteomalacia: A retrospective analysis of 144 cases," *Endocrine Journal*, 64(7), pp. 675–683. Available at: https://doi.org/10.1507/endocrj.ej16-0587.